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CASE REPORT

Pseudoprogression after proton beam irradiation for a choroid plexus carcinoma in pediatric patient: MRI and PET imaging patterns

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Abstract
Purpose Pseudoprogression is a rare complication of radiation therapy, and discrimination between true progression and pseudoprogression is of paramount importance for further medical care. We present a case of intra-axial pseudoprogression following complementary proton radiation therapy for a choroid plexus carcinoma in a child. We aim to highlight radiological patterns of pseudoprogression after proton beam therapy.
Case report A 6-year-old girl presented with choroid plexus carcinoma, manifesting as change in behavior, tremor, and balance disorder. Partial resection and chemotherapy were performed. Complementary localized proton beam therapy (54 Gy) was administered on the residual tumor. Eight month follow-up MRI showed an abnormal, irregular, rim-like enhancement in the pons and both temporal lobes within the field of irradiation. These lesions had a low cerebral blood volume (CBV) on perfusion MR imaging and no restricted diffusion. However, the lesions were hypermetabolic on O-(2-[18F]fluoroethyl)-L-tyrosine (FET)-PET MRI. Follow-up MRI showed disappearance of these lesions confirming the perfusion MR diagnosis of pseudoprogression.
Conclusion Based on this case, radiological patterns of pseudoprogression after proton beam therapy may be a low CBV and no restricted diffusion. Lesions can be hypermetabolic on FET-PET imaging.

Keywords Radiotherapy · Proton · Tumor · Radiation injury · MRI · PET

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Introduction

Proton beam therapy (PBT) is an emerging and promising technique in neuro-oncology. Its fundamental principles originate from particle physics research during World War II, which led to the development of the early charged particle radiation therapy devices. The dosimetric characteristics of protons allow the delivery of a high-dose radiation in a limited area of the body [1].

Today, proton beam therapy has shown benefits in the treatment of skull base tumors, pituitary adenomas, acoustic neuromas, uveal melanoma, optic pathway gliomas, and nasopharynx, paranasal sinuses, and spinal cord tumors [1].

Pseudoprogression is a rare complication of radiation therapy consisting of new abnormal enhancing lesions appearing often within 2 months after the completion of radiochemotherapy and resolving spontaneously without any treatment [2]. The incidence of pseudoprogression after conventional photon therapy ranges from 5 to 24 % [3, 4]. Many previous studies have described pseudoprogression after photon radiation therapy associated with temozolomide chemotherapy for glioblastoma in adults. Subacute radiation

injury in childhood gliomas treated by conventional radiotherapy with or without chemotherapy has also been described [5, 6], but only one case of pseudoprogression after PBT for an intra-axial low-grade glioma in a teenager has been reported so far [7]. The discrimination between pseudoprogression and tumoral progression is a radiological challenge and is of great importance for further medical care.

We present a case of intra-axial pseudoprogression following adjuvant proton radiation therapy for a choroid plexus carcinoma. We aim to highlight radiological patterns of pseudoprogression after proton beam therapy in a pediatric case.

Case

A 6-year-old girl, with unremarkable medical and family history, presented with behavior changes, tremor, and balance disorder. Neurological and ophthalmological examinations showed ataxia with a widened base, bilateral papillary edema, decreased visual acuity (6/10 on Snellen chart), and concentric visual field narrowing. The initial brain MRI showed hydrocephalus and a large and heterogeneous mass centered on the left lateral ventricle (Fig. 1). This mass had a mixed tissular and cystic composition with strong and heterogeneous enhancement after gadolinium administration. The lesion was surrounded by parenchymal edema. The patient underwent partial surgical resection of the lesion with ventriculoperitoneal shunt placement. Cerebrospinal fluid was free of any abnormality. The postoperative histological diagnosis was OMS grade III choroid plexus carcinoma. A six-course chemotherapy according to the protocol SIOP-CPT-2000, comprising carboplatin, etoposide, and vincristine, was administered from October to July 2010. Proton beam radiation therapy (PBT) was administered from March to May 2010 at a total dose of 54 Gy on the residual tumor. She then received temozolomide from October to December 2010 (1 month and 11 days). The MRI follow-up (1.5 T) 8 months after the start of radiation therapy showed the appearance within the field of irradiation of abnormal heterogeneous enhancements in the pons and in both temporal lobes with rim-like appearance. The lesions were hyperintense on T2W and FLAIR and hypointense on T1W (Figs. 2 and 3). At this point, the differential diagnosis was tumoral relapse versus pseudoprogression. An FDG PET was performed and showed no hypermetabolism, in particular within the abnormal enhancements. Then, a O-(2-[18F]fluoroethyl)-L-tyrosine (FET)-PET MRI was performed and showed a clear hypermetabolism in the lesions of the pons and the left temporo-polar lobe orienting the diagnosis toward tumor recurrence. PET acquisitions were performed on a hybrid PET/MRI tomograph (Philips Ingenuity TF PET/MR 3 T). However, at MRI, there was no restricted diffusion on diffusion-weighted imaging (DWI) and the lesions presented a low cerebral blood volume (CBV) on the perfusion sequence, indicating radiation-induced modifications.

The follow-up MRI at 11 and 29 months (Figs. 2 and 3) showed disappearance of the lesions and confirmed the diagnosis of pseudoprogression. The patient has kept postoperation sequelae such as complete blindness as well as frequent complex partial seizures controlled by medication. The last follow-up MRI (26 months since the end of PBT) showed no sign of relapse.

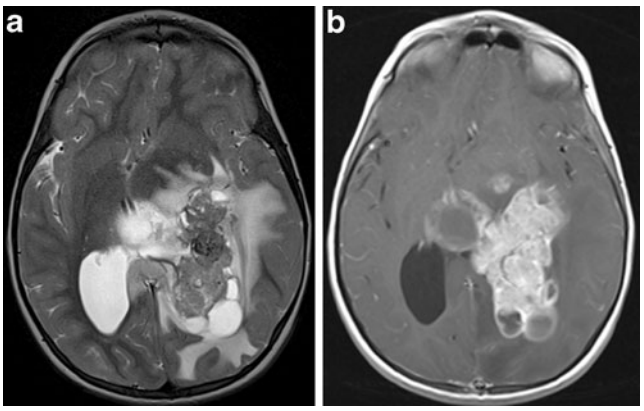

Fig. 1 Brain MRI at presentation: axial T2-weighted image (**a**) and T1-weighted image after gadolinium administration (**b**) showing a large and heterogeneous mass centered on the left lateral ventricle, with tissular and cystic components, strong and heterogeneous enhancement, mass effect, and perifocal parenchymal edema. Histological diagnosis was OMS grade III choroid plexus carcinoma

Discussion

To our knowledge this is the first reported case of intra-axial pseudoprogression following proton beam therapy of an extra-axial ventricular tumor in a pediatric patient. In the presented case, diagnosis of pseudoprogression was confirmed by the disappearance of lesions on MRI follow-up.

Lesions were located bilaterally within the field of irradiation and appeared 8 months after the beginning of PBT. The time of occurrence of pseudoprogression in our case is delayed in comparison to the 2 months described in the literature for adult gliomas treated by photon radiation therapy and chemotherapy [2, 5, 8]. However it is concordant with the only report of pseudoprogression after exclusive PBT of a partially resected low-grade glioma in a teenager by Meyzer and colleagues [7] who described a lapse of 6 months. Since our patient has been treated by chemotherapy and PBT, and the case reported in the literature has been

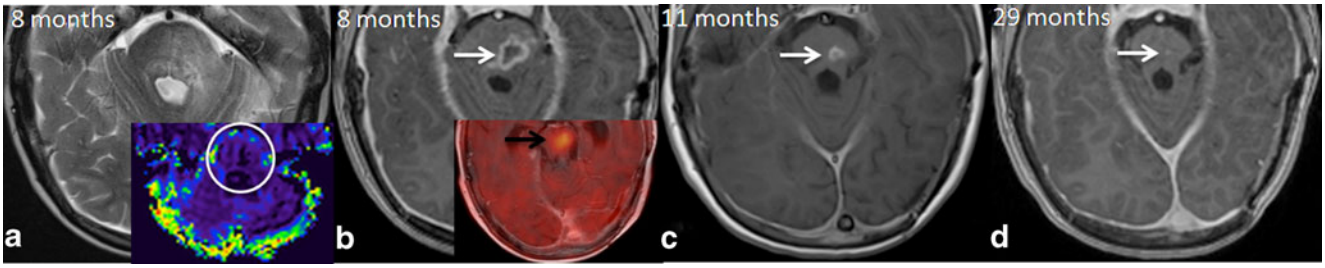

Fig. 2 Follow-up MRI 8 months (**a**, **b**), 11 months (**c**), and 29 months (**d**) after beginning of complementary proton beam irradiation. **a** Axial T2-weighted showing an hyperintense lesion within the pons. **b** Axial T1-weighted after gadolinium showing appearance of abnormal rim-like enhancement (*white arrow*) with T2 hypersignal (**a**). The lesion shows a low CBV (*circle*, **a**) and is hypermetabolic on FET-PET/MRI (*black arrow*, **b**). Follow-up MRI at 11 and 29 months shows almost disappearance of the lesion (*white arrows*, **c**, **d**) confirming the diagnosis of pseudoprogression

treated exclusively by PBT after surgery [7], we can assume that the late appearance of pseudoprogression is related to the use of PBT.

The lesions appeared hypointense on T1W and hyperintense on T2W and FLAIR which is not specific. The relevant MRI characteristics of these lesions are a low CBV on the dynamic susceptibility contrast perfusion MR imaging and absence of restricted diffusion on DWI. Our findings are concordant with the literature, as Kang and colleagues have shown that new lesions with restricted diffusion (low ADC values) after radiosurgery for brain intra-axial metastasis are more likely to be recurrent tumors than radiation-induced injury [9]. Regarding CBV, our findings are in further agreement with Essig and colleagues [10] who have shown that a low CBV value is suggestive of tumor response in a group of 18 patients with treated brain metastasis. Our findings are also concordant with the study of Hoefnagels and colleagues who showed that high relative CBV is suggestive of tumor recurrence in a group of 20 tumor recurrences and 14 tumor necrosis following brain metastasis treated by stereotaxic radiosurgery [11].

These studies are related to pseudoprogression after photon radiation therapy of intra-axial tumors and found similar imaging characteristics in our case of extra-axial tumor treated by proton radiation therapy in a child. So we can suppose that pseudoprogression is a process which seems unrelated to the type or location of the primary tumor, and independent of the patient age, and its imaging patterns are a low CBV with no restricted diffusion.

In our case, FET-PET imaging showed hypermetabolism in two out of three lesions and was suggestive of tumor progression, so it did not help to diagnose pseudoprogression. Many studies support that amino acid tracers, such as FET and 11C-methionine, might be a valuable modality to differentiate between tumor recurrence and pseudoprogression [12, 13]. In the latter studies, however, the primary tumors were intra-axial gliomas treated by photon radiation therapy, in opposition to our case describing a ventricular extra-axial tumor treated by proton radiation therapy. In agreement with our results, there are a few reports showing PET positive findings in radiation necrosis lesions [14, 15]. The discrepancy of results regarding PET imaging findings can possibly be explained by the different location of primary tumor and/or the radiation modality. Presumably, the uptake intensity could support differential diagnosis, but large series are required in order to validate a specific cutoff.

Analysis of CBV and diffusion-weighted imaging is helpful in the differential diagnosis of relapse versus radiation injury. Based on this case, it may be suggested that low CBV and absence of restricted diffusion are patterns of pseudoprogression, while FET-PET can be positive in these cases.

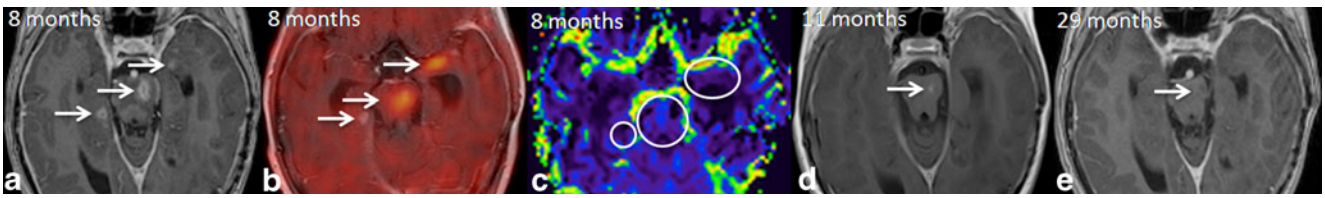

Fig. 3 Follow-up MRI 8 months (**a**–**c**), 11 months (**d**), and 29 months (**e**) after beginning of complementary proton beam irradiation showing appearance of abnormal rim-like enhancements on T1W after gadolinium within the pons and both temporal lobes (*arrows*, **a**). The lesions show a low CBV (*circles*, **c**) and two of them are hypermetabolic on FET-PET/MRI (*arrows*, **b**). Follow-up MRI at 11 and 29 months shows disappearance of temporal lesions and almost disappearance of the pontine lesion (*white arrows*, **d**, **e**) confirming the diagnosis of pseudoprogression

Conflict of interest No competing interest.

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